

**AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/565,669 (Q92767)**

REMARKS

Claims 1-15 and 17 are in the application. Solely to compact prosecution, and without prejudice or disclaimer, Applicants amend claims 1, 5, 9, 11, 13 and 15 for grammar and/or dependency. In light of Applicants' amendments for dependency, Applicants add new claims 23-29. Support for new claims 23-29 is found in original claims 4, 8, 9, 10, and 13-15. No new matter is added. Entry and consideration of the Amendment is respectfully requested. Applicants expressly reserve rights to all unclaimed subject matter.

Applicants thank the Examiner for acknowledgement of receipt of the priority documents and acceptance of the drawings.

I. Acknowledgement of the IDSs Submitted January 24, 2006 and February 5, 2009 is Requested

At page 2 of the partially acknowledged IDS (PTO/SB/08) submitted January 24, 2006, the Office struck-through foreign patent document JP 5-172810 published July 13, 1993 (Kagaku Gijusuchō Hoshasen et al.) indicating that the document was not considered.

Applicants' IDS is proper under 37 C.F.R. 1.56 (c) and 1.98(a)(3) (i.e., complies with the concise explanation requirement vis-à-vis the International Search Report submitted therewith accompanied by the English translation of Kagaku Gijusuchō Hoshasen et al.). *See* MPEP 609.04(a).

Acknowledgement of the IDS filed February 5, 2009 and foreign patent document JP 5-172810 published July 13, 1993 (Kagaku Gijusuchō Hoshasen et al.) is respectfully requested.

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II. Claims 13 and 15 Are Proper Under 37 C.F.R. § 1.75(c)

At page 2 of the Office Action, the Office objects to claims 13 and 15 under 37 C.F.R. § 1.75(c) as being in improper form.

Solely to compact prosecution, and without prejudice or disclaimer, Applicants' herewith amend claims 3, 7, 9 and 13 for dependency. Claims 13 and 15 are proper.

Withdrawal of the objection to claims 13 and 15 is respectfully requested.

III. Claims 1-15 and 17 Are Patent Eligible Under 35 U.S.C. § 101

At page 3 of the Office Action, the Office rejects claims 1-15 and 17 under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter. The Office relies solely on *In re Bilski* (*In re Bilski*, 545 F.3d 943 (Fed. Cir., 2008)) to support the rejection, asserting that any method claim under any circumstance in any area of technology must meet the “machine-or-transformation test” in order to be patent eligible under 35 U.S.C. § 101. The Office explicitly applies this reasoning to the present application indicating, “[I]n the instant case, the method claims are not so tied to another statutory class of invention because the method steps that are critical to the invention are ‘not tied to any particular apparatus or machine’, and therefore do not meet the machine-or-transformation test as set forth in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).”

The Office is incorrect on the law. *In re Bilski* is not applicable to Applicants' invention. The Opinion referred to by the Examiner involves a method of hedging risks in commodities trading, not a method for evaluating chromosome state and evaluation systems. Judge Michel,

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the author of the Opinion, indicated, *Bilski* did not discuss those areas of art and the facts did not provide an opportunity to address those arts (referring specifically to business methods, software and bioinformatics, and thus, biotechnology and chemistry). *BNA Journal*, Number 139, July 23, 2009, ISSN 1522-4325, TODAY'S UPDATE, Conferences, "Chief Judge Michel Says Commentary Reading Too Much Into *Bilski* Opinion", attached herewith. Judge Michel commented that the Opinion was never intended to be applied rigidly or restrictively as to invalidate patents for whole areas of technology thereby significantly limiting the application of his Opinion and the holding in *Bilski*. *Id.* Thus, the Office applied the wrong law, rigidly and restrictively applied incongruent law and/or improperly broadened the holding in *In re Bilski* in making the present rejection because Judge Michel, the author of the Opinion, indicated, *Bilski* did not discuss the art at issue and the facts did not provide an opportunity to address this art.

Withdrawal of the rejection is therefore respectfully requested.

IV. Claims 1-15 and 17 Are Definite Under 35 U.S.C. § 112, Second Paragraph

At page 4 of the Office Action, the Examiner rejects claims 1-15 and 17 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "by measuring a desired area of said cells in information of a plurality of images formed from a plurality of pixels," more specifically because allegedly "in information" is unclear.

The law is settled. The essential inquiry is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim

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interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. It is necessary to consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. *See, e.g., Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000); *In re Larsen*, No. 01-1092 (Fed. Cir. May 9, 2001); *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, (Fed. Cir. 2004). Only if the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. *See Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

Applicants disagree with the Office that “in information” is unclear. In light of the specification, the art, and the plain meaning of the language of the claim from the perspective of one possessing ordinary skill in methods for evaluating chromosome state and evaluation systems thereof, “in information” clearly refers to a plurality of images formed from a plurality of pixels having an attribute value (i.e., claim 1). A person of ordinary skill in the art can interpret the metes and bounds of the claims. The Office’s comment goes to the breadth of the claims however, the breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689 (CCPA 1971). The scope of the subject matter embraced by the claims is clear thus, the claims comply with 35 U.S.C. 112, second paragraph. *See also* MPEP § 2173.04.

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However, solely to advance prosecution, and without prejudice or disclaimer, Applicants herewith amend the claims to recite, “a desired area of said cells from information obtained from a plurality of images...” (e.g., claim 1).

Withdrawal of the rejection is therefore respectfully requested.

V. Claims 1-15 and 17 Are Patentable Under 35 U.S.C. § 103

At page 5 of the Office Action, the Office rejects claims 1-15 and 17 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Parada et al. (Trends in Cell Biology, 12(9):425-432 (2002)) in view of U.S. Patent No. 7,136,540 (Kiyuna). The Office admits that Parada et al. fail to teach statistical imaging techniques used in the microscopic analysis. The Office concludes that it would have been obvious to use the imaging techniques of Kiyuna with the microscopic evaluation of chromosome territories, as taught by Parada et al. and that one would have had a reasonable expectation of success in doing so because imaging statistical techniques are well known in the art for evaluation of cell and cellular structures and Parada et al. is a generalized method for extracting a target object region from image data. Id.

To maintain a rejection under 35 U.S.C. §103, the cited references must teach or suggest each and every element of the claim. It is necessary to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some *articulated reasoning* with some *rational underpinning* to support the legal conclusion of obviousness. The combination of familiar elements according to known methods

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is likely to be obvious when it does no more than yield *predictable* results. As reiterated by the Supreme Court, an analysis for determining obviousness must include analysis of the underlying factual inquiries including, (1) determining the scope and content of the prior art; (2) ascertaining the differences between the claimed invention and the prior art; and (3) resolving the level of ordinary skill in the pertinent art. *Id.* It is well-settled law that a *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. See *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

Applicants disagree with the Office. The Office's conclusion of obviousness is premised on technical information allegedly taught in Parada et al. however, the Office is incorrect. For example, the Office alleges that the reference teaches visualization of chromosomes in interphase, that functional roles may be elucidated from the disclosed visualizations and that this information is extremely useful in cancer detection. Office Action, page 6. However, Parada et al., when read in its proper context, illustrates the opposite.

Parada et al. make clear that as of the references' publication date the state of the art of chromosome territory measurement is highly unpredictable, nascent and unrealized. For example, the reference states, "The size of a chromosome territory is roughly determined by its DNA content but is also affected by other factors such as its overall transcriptional status [12,13]...the internal organization of chromosome territories is still unclear...". Parada et al., page 425. The reference states, "the chromatin fibre within chromosome territories *has been suggested* either to exist in the form of loops of 30-150 kb, which in turn form rosettes to give the 1 Mb replication domains, or to form ~3 Mb giant loops that are generated by a random walk

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of the fibre and are held together at their bases [18,19].” [Emphasis added] Parada et al., pages 425-426. The reference states, “Chromosome movements are *probably* also restrained by internal nuclear structures (Fig. 3a). Nuclear matrix-attachment regions have been identified along the entire length of chromosomes, although the protein-binding partners of matrix-attachment regions have been *elusive* [56]. The recent observation that lamina are not restricted to their role as the major constituent of the lamina but are also found throughout the nuclear interior allowing for the interesting *possibility* that chromosomes interact with and *might be* tethered by internal lamina [57].” [Emphasis added] Parada et al., page 428. Further, Parada et al. states, “However, in none of these cases has simultaneous association of multiple chromosomes or direct physical tethering with any nuclear body been demonstrated” and “Despite these cases of observed correlation between recruitment of loci to heterochromatin and silencing, it is not clear whether recruitment to heterochromatin causes silencing or is merely a consequence of gene silencing.” Parada et al., page 429.

The reference as cited by the Examiner states, “If chromosome positioning were functionally important for the regulation of gene expression programs, one would predict that chromosome arrangements should undergo changes as gene-expression profiles of cells change during differentiation and development. Only very limited experimental data are available to test this prediction.” Parada et al., page 429. Similarly, the reference states, “The non-random positioning of chromosomes in the interphase nucleus *has implications* for the formation of chromosome translocations.” [Emphasis added] Id.

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The concluding remarks in Parada et al. are critical to understand the reference but were not referred to in the Office Action. The concluding remarks state, "Chromosomes are arranged non-randomly within the cell nucleus. However, we have only a *rudimentary* understanding of the patterns by which they are organized, how these patterns are established and maintained, and, most importantly, what the functional implications of chromosome positioning are. It is astonishing to realize that, now that genomes are routinely sequenced, we still do *not* understand the spatial organization of chromosomes." [Emphasis added] Parada et al., page 430.

Kiyuna fails to teach or suggest Applicants' methods for evaluating chromosome state and evaluation systems thereof. The deficiencies of Parada et al. are not cured by Kiyuna. The portion of Kiyuna referred to by the Examiner is not the method recited in Applicants' claims (i.e., claim 1). Office Action, pages 6-9.

The Examiner failed to establish a *prima facie* case of obviousness because the Office failed to set forth any credible evidence or point out any suggestion in the cited references of Applicants' recited method - in fact, Parada et al. indicates the opposite of that which the Office concludes - nowhere is it indicated that it was at all conventional in the art to arrive at the proposed combination. The Examiner failed to provide a sufficient reason or explicit analysis of why the disclosures of the references should be combined. There is no suggestion to combine the teachings and suggestions of Parada et al. and Kiyuna, a speculation advanced by the Examiner, except from using Applicants' invention as a template through a hindsight reconstruction of, for example, claim 1, which is legally forbidden. The Office's obvious analysis failed to include analysis of the underlying factual inquiries (i.e., the scope and content

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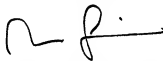
of the prior art was not properly considered thus, the differences between the claimed invention and the prior art could not possibly have been accurately determined). The law is clear that rejections on obviousness grounds *cannot* be sustained by mere conclusory statements and *cannot* be sustained using knowledge which was beyond the level of ordinary skill in the art at the time the claimed invention was made by including knowledge gleaned only from Applicants' disclosure - a strategy presently employed by the Office in asserting obviousness.

Withdrawal of the rejection is therefore respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The U.S. Patent and Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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